## CASE REPORT

# AUROLAB AQUEOUS DRAINAGE IMPLANT IN YOUNG ADULT WITH NEOVASCULAR GLAUCOMA AND TUBERCULOSIS HISTORY: A CASE REPORT

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#### ABSTRACT

**Introduction:** Neovascular glaucoma (NVG) is historically known as rubeotic glaucoma, from "rubeosis iridis" that refers to the iris neovascularization. One of several causes that lead to rubeosis iridis is changes in Pigment Epithelium-Derived Growth Factor (PEDF) that may be caused by Mycobacterium tuberculosis. The influence of NVG may cause intraocular pressure (IOP) to rise rapidly. It can be decreased by Aurolab Aqueous Drainage Implant (AADI).

**Case Report:** A 34-year-old male complained of left eye pain and sudden decreased vision for the past 2 months. He had been diagnosed with tuberculosis since 8 months ago. The patient's blood pressure, blood sugar, cholesterol, and triglycerides were within normal limit. Diabetes Mellitus (-). Human Immunodeficiency Virus (-). Visual acuity of left eye was hand movement. The pupil was dilated and non-reactive, anterior chamber depth is shallow, and rubeosis iridis (+). IOP is 60 mmHg. Medical management was failed to decrease the IOP. Funduscopy image showed cup-disc ratio was 0,7. Ganglion cell complex parameters showed 80,91. On the next day after AADI implantation surgery, the patient's left eye IOP was reduced to 10 mmHg. On the 14<sup>th</sup> day post operative visual acuity was 2 meter counting finger. The anterior segment of the conjunctiva bulbi was hyperemic and conjunctival injection was reduced. The camera oculi anterior showed remainder of the implant. In the iris, rubeosis iridis disappeared, pupil was dilated, IOP was increased to 12 mmHg

**Discussion:** Neovascular glaucoma was caused by the growth of the fibrovascular membrane on the surface of the iris and the anterior chamber angle. The three most common causes of neovascular glaucoma were diabetes mellitus, central retinal vein occlusion, and carotid artery occlusion.

**Conclusion:** AADI is a safe and effective option for patients with neovascular glaucoma following tuberculosis.

Keywords: AADI, Neovascular glaucoma, Tuberculosis

## INTRODUCTION

urolab Aqueous Drainage Implant (AADI) is an implant with a non-valved tube used to achieve the targeted intraocular pressure (IOP). It was made of a high-purity silicones NuSil that has passed tissue culture cytotoxicity testing. Indication of AADI implant which is including Neovascular glaucoma. Neovascular glaucoma is a secondary angle-closure glaucoma which associated with rubeosis iridis. It was reported that the incidence rates rubeosis iridis of Neovascular Glaucoma (NVG) in the first six months after surgery were 10-23%.<sup>1-5</sup>

NVG may show a fibrovascular membrane developing along the blood vessels that are formed. Therefore, the peripheral iris is pulled into the anterior chamber, resulting in peripheral

anterior synechiae, and subsequently inhibiting the outflow of aqueous humor and increasing IOP.<sup>6-8</sup> The most widely used theory in NVG is the presence of retinal ischemia, which releases angiogenic factors that diffuse forward.<sup>7,8</sup> Although hypoxia is believed to be the main trigger of angiogenesis, other factors also play a role in the formation of abnormal blood vessels. Inflammatory mediators such as angiopoietin-1 and angiopoietin-2 have been shown to play a role in the formation of new vessels and remodeling, which is similar with the role of inflammatory process.<sup>7,9</sup>

Biomicroscopy of the anterior chamber in NVG shows the presence of cells and flares. Gonioscopy shows new vessels growing from the circumferential artery of the ciliary body to the surface of the iris and onto the surface of the angular wall.<sup>7,8</sup> The study described the Aurolab Aqueous Drainage Implant insertion to decrease the IOP, reduce rubeosis iridis, and increase the visual outcome in a young adult.

#### **CASE ILUSTRATION**

A 34-year-old male patient came to the Medan Baru Eye Hospital on 18 December 2017 with chief complaint of blurred left eye vision accompanied by pain and redness since 4 days before admission. Patients often experience recurrent pain in the left eye for the last 2 months. The pain was followed by a decreased visual acuity, and he could only detect object motion. The patient denied ever having nausea and vomiting accompanied by severe headaches. The patient admitted that he tried to drip betel leaf juice on his left eye, but there was no improvement. The patient had a history of pulmonary tuberculosis and had undergone anti-tuberculosis drugs for 8 months. The patient had a history of smoking 10 cigarettes per day. The patient denied having experienced trauma to the left eye before. He also denied any history of diabetes and hypertension.

Physical examination was performed. The patient's blood pressure, blood glucose, cholesterol, and triglycerides of the patient were within normal limits. Human Immundeficiency Virus (HIV) test result was negative. Visual acuity was 20/20 in the right eye and hand movement in the left eye. IOP was 10 mmHg in the right eye and 31 mmHg in. the left eye. Anterior segment examination of the right eye was normal and the posterior segment examination was normofundus. Tarsal and bulbar conjunctival hyperemia, also conjunctival injection was found in the left eye. The anterior chamber angle was narrow. Gonioscopy showed grade II angle closure in the left eye. Rubeosis iridis can be seen in the left eye. Pupils were not equally reactive, with dilated left eye pupil and negative light reflex (Figure 1). From the funduscopy examination (Figure 2), cup-to-disc ratio (CDR) was obtained to be 0,4 in the right

eye and 0,7 in the left eye. Further diagnostic examination was performed using optical coherence tomography (OCT) (Figure 3) and ocular ultrasound (Figure 4). The patient was diagnosed with neovascular glaucoma in the left eye. The patient was planned to undergo Aurolab Aqueous Drainage Implant (AADI) implantation surgery. Mannitol 25% 1-2 g/kg body weight was given as a pre-operative medication. IOP after mannitol administration was 30 mmHg. The right eye was within normal conditions.



Figure 1. The patient's left eye.



Figure 2. Funduscopic examination of the right and left eye



Figure 3. Optical coherence tomography of glaucoma

In OCT glaucoma examination with 7/10 signal strength with test type ONH/GCC Symmetry Analysis Report, Centration (+) and aligned. Retinal nerve fiber layer (RNFL) thickness in the right eye was relatively good in superior, inferior, nasal and temporal segment, while in the left eye only ganglion cell complex (GCC) thickness was obtained. Mean GCC of the right eye was 92.62, and 80.91 in the left eye. Superior GCC of the right eye was 89.94, and 95.86 in the left eye. Inferior GCC of the right eye was 95.36, and 66.43 in the left eye. There was significant thinning in GCC of the left eye.



Figure 4. Ultrasound of the left eye.

In ultrasound examination that was done axially, there was lens with no increased spike, no membrane or mass in the vitreous, retina was intact, no increased thickness of choroid and optic nerve was within normal spike, with negatif after movement (Figure 4).

Surgical technique for AADI consisted of a fornix-based or limbal-based conjunctival incision to create a conjunctival flap between 2 rectus muscles, generally in the superotemporal quadrant. Body implant was positioned 8–10 mm from the limbus, outside limbal healing space. The plate was then sutured to the sclera with a 9.0 or 10.0 nylon suture. The drainage tube was trimmed to permit a 2–3 mm insertion in the anterior chamber and was bevel cut to an angle of 30°, to facilitate AC entering. An anterior chamber paracentesis was performed, and viscoelastic substance was injected to increase space. The anterior chamber was then entered 1–3 mm posteriorly to the corneoscleral limbus with a 22–23G needle. The needle tract was anterior and parallel to the plane of the iris. The tube, which was trimmed so that the bevel faces to the corneal endothelial surface, was inserted into the anterior chamber through the needle tract. Care must be taken at this point to ensure that the drainage tube did not contact iris or corneal endothelium after insertion.



Figure 5. Implantation of Aurolab Aqueous Drainage Implant.



**Figure 6.** Post-operative day 1<sup>st</sup> (left) and day 14<sup>th</sup> (right) after Aurolab Aqueous Drainage implant implantation surgery.

On the next day after AADI implantation surgery on the left eye (Figure 5). The anterior segment of the conjunctiva bulbi was hyperemic and conjunctival injection was reduced. The camera oculi anterior showed the remainder of the implant. Left eye IOP was reduced to 10 mmHg. The post-operative medications include ciprofloxacin 500 mg twice a day,

methylprednisolone 4 mg three times a day, vitamin B once a day, tobramycin 0.3% + dexamethasone 0.1% one drop four times a day in the left eye, and tropicamide 0.5% one drop four times a day in the left eye.

Post operative drugs were given until day 14<sup>th</sup> (Figure 6). After 14 days of therapy, the patient's condition has improved, visual acuity was 2 meter counting finger in the left eye. In the iris, rubeosis iridis had disappeared, pupil was dilated, and IOP was increased to 12 mmHg.

### DISCUSSION

Neovascular glaucoma was caused by the growth of the fibrovascular membrane on the surface of the iris and the anterior chamber angle. The three most common causes of neovascular glaucoma were diabetes mellitus, central retinal vein occlusion, and carotid artery occlusion.<sup>7,9</sup> However, after carrying out a series of examinations on this patient, it was found that the patient had a history of pulmonary tuberculosis and had received anti-tuberculosis treatment for 8 months. According to the notable theory, *Mycobacterium tuberculosis* could activate pro-inflammatory factors such as pigment epithelium-derived growth factor (PEDF), where PEDF could trigger iris neovascularization in neovascular glaucoma.<sup>10,11</sup>

Anti-inflammatory cells such as PEDF that developed from tuberculosis increase C-reactive protein and pro-inflammatory cells such as IL-6 and other cytokines. When the inflammatory cells increased sharply, it causes a toll-like receptor (TLR)-2 to be detected with high levels of CD16+ which was related to tumor necrosis factor (TNF)- $\alpha$ . Activation of TLR-2, CD16+, and secretion of pro-inflammatory cytokines are the initial processes of inflammatory reactions in the retina. Increased levels of oxidative stress could also found in the vitreous, erythrocytes, platelets, and monocytes. That resulted to free radical damage to DNA and protein which was indicated by the accumulation of 8-hydroxy-2'-deoxyguanosine in leukocytes and nitrotyrosine in monocytes.<sup>12-14</sup>

Nitrosative stress was also reported to increase, followed by increased levels of iron and copper, which also suppresses zinc so that iron level dropped dramatically. When the processes happened, an interaction between TNF- $\alpha$  and matrix metalloproteinase (MMP)-9 in various cells would occur. This process initiated the inflammatory process for the mechanism for angiogenesis.<sup>15-17</sup> PEDF was a glycoprotein and inhibitor that has the potential to cause ischemia and trigger neovascularization. This reduction in PEDF had been widely reported in patients with both proliferative and non-proliferative diabetic retinopathy. The decrease in PEDF affected the levels of Vascular Endothelial Growth Factor (VEGF) and Vascular Endothelial Growth Factor Reseptor (VEGFR) in many patients with tuberculosis and Chronic Obstructive Pulmonary Disease (COPD).<sup>18-21</sup>

At the initiation of therapy, this patient was given drugs to suppress the production of aqueous humor, such as beta-blockers, carbonic anhydrase inhibitors, and alpha-receptor blockers. Systemic carbonic anhydrase inhibitors should be used with caution, especially in patients with chronic pulmonary disease, electrolyte disorders, kidney disease, and diabetes mellitus. This patient was given acetazolamide 250mg two times a day and betaxolol 0.5% three times a day. Glaucoma drugs given at the beginning of the therapy were only able to reduce IOP by 7 mmHg (from 60 mmHg to 53 mmHg). Theoretically, acetazolamide was a group of carbonic anhydrase inhibitors that could reduce IOP by 15-20%, and beta-blockers can reduce IOP by 15-25%, but these results were contrary with the results obtained in patients, therefore, it was advisable to perform AADI implantation without panretinal photocogulation because there was no diabetic history on this patient. <sup>22-24</sup>

Pre-operative use of mannitol was given to the patient before the AADI implantation surgery. Mannitol was an effective hyperosmotic drug to lower IOP. It was reported that after the administration of mannitol, the patient's IOP was decreased to 30 mmHg, and the mannitol infusion was still attached during surgery.<sup>21,23</sup> AADI (Aurolab Aqueous Drainage Implant) was an implant that had a non-valved tube that used to achieve the targeted IOP. AADI was made of NuSil permanent implant silicone elastomer that had passed tissue culture cytotoxicity test. Its surface area is 350 mm, the lateral wings were designed to be positioned under the rectus muscle. The AADI had fixation holes to suture the plate about 10 mm at the back of the limbus. AADI had been commercially available in India since 2013 and was similar to Baerveldt's glaucoma implant.<sup>25</sup> The patient's IOP is shown in Figure 7.



Figure 7. Line chart of intraocular pressure (IOP) over time. This graph shows decreased IOP after surgery.

## CONCLUSION

The advantage of AADI is that this implant can result in a stable IOP because the AADI surface is large enough to maintain the hemodynamics of the aqueous humor, reduce rubeosis iridis to providing better visual outcome. The second is in terms of cost, AADI is much more economical compared to other devices such as Baerveldt or Ahmed Valve.

#### REFERENCES

- 1. Rhee D.J, Nicholl. Secondary Angle Closure Glaucoma. Glaucoma. 2003;17:326-328.
- 2. Khan Y.A. Glaucoma Neovascular. 2006.
- 3. Vaughan, Asbury S. Neovascular Glaucoma. General Ophthalmology 6th Ed. 2006;212-27.
- William L & Wilkins. 2005. Glaucomas Associated With Disorder of the Retina, Vitreous and Choroid in Shields. Glaucoma 5<sup>th</sup> Ed; 2005. 19: pp. 328-37.
- 5. American Academy of Ophthalmology. Basic and Clinical Science Course section 10: Glaucoma. San Fransisco : American Academy of Ophthalmology. 2018.
- 6. Mosby. Mosby's Medical Dictionary, Amsterdam: Elsevier 8<sup>th</sup> Ed; 2008.
- 7. Ilyas S, Tanzil M. Glaukoma. Ilmu Penyakit mata 3rd Ed. Jakarta: Balai Penerbit FKUI; 2006. p.212-18
- 8. Wijaya N. Glaukoma Sekunder. Ilmu Penyakit Mata. Jakarta : Balai Penerbit FKUI; 2008; 219-44.
- 9. Bertamian M. Glaucoma Neovascular in Clinical Guide to Glaucoma Management. Amsterdam: Elsevier; 2004;263-9.
- 10. Madhavan HN, Therese KL, Kavitha D. Further investigations on the association of Mycobacterium tuberculosis with Eales' disease. Indian J Ophthalmol. 2002; 50:35–39.
- 11. Bhutto IA, McLeod DS, Hasegawa T, et al. Pigment epithelium-derived factor (PEDF) and vascular endothelial growth factor (VEGF) in aged human choroid and eyes with age-related macular degeneration. Exp Eye Res. 2006;82(1):99-110.
- 12. Saxena S, Pant AB, Khanna VK, et al. Interleukin-1 and tumor necrosis factor-alpha: novel targets for immunotherapy in Eales disease. Ocul Immunol Inflamm. 2009;17(3):201-206.
- 13. Sen A, Chowdhury IH, Mukhopadhyay D, et al. Increased Toll-like receptor-2 expression on nonclassic CD16+ monocytes from patients with inflammatory stage of Eales' disease. Invest Ophthalmol Vis Sci. 2011;52(9):6940-6948.
- 14. Cosgrove GP, Brown KK, Schiemann WP, et al. Pigment epithelium-derived factor in idiopathic pulmonary fibrosis: a role in aberrant angiogenesis. Am J Respir Crit Care Med. 2004;170(3):242-251.
- 15. Liu JT, Chen YL, Chen WC, et al. Role of pigment epithelium-derived factor in stem/progenitor cellassociated neovascularization. J Biomed Biotechnol. 2012:871272.
- 16. Li X, Wang T, Yang T, et al. Elevated plasma levels of pigment epithelium-derived factor correlated with inflammation and lung function in COPD patients. Int J Chron Obstruct Pulmon Dis. 2015;10:587-594.
- Ogata N, Tombran-Tink J, Nishikawa M, et al. Pigment epithelium-derived factor in the vitreous is low in diabetic retinopathy and high in rhegmatogenous retinal detachment. Am J Ophthalmol. 2001;132(3):378-382.
- 18. Boehm BO, Lang G, Volpert O, et al. Low content of the natural ocular anti-angiogenic agent pigment epithelium-derived factor (PEDF) in aqueous humor predicts progression of diabetic retinopathy. Diabetologia. 2003;46(3):394-400..
- 19. Angayarkanni N, Selvi R, Pukhraj R, Biswas J, Bhavesh SJ, Tombran-Tink J. Ratio of the vitreous vascular endothelial growth factor and pigment epithelial-derived factor in Eales disease [published correction appears in J Ocul Biol Dis Infor. 2009 Jun;2(2):94]. J Ocul Biol Dis Infor. 2009;2(1):20-28.
- Tiwari A, Trivedi AC, Srivastava P, Pant AB, Saxena S. Comparative modeling of retinol-binding protein-3 and retinal S-antigen in Eales' disease and prediction of their binding sites using computational methods. J Ocul Biol Dis Infor. 2010;3(3):88-91
- 21. Li X, Wang T, Yang T, Shen Y, An J, Liu L, Dong J, Guo L, Li D, Zhang X, Chen L, Xu D, Wen F. Elevated plasma levels of pigment epithelium-derived factor correlated with inflammation and lung function in COPD patients. *Int J Chron Obstruct Pulmon Dis.* 2015;10(1):587-594.
- 22. Mishra A, Luthra S, Baranwal VK, Parihar JK. An interesting case of rubeosis iridis with neovascular glaucoma in a young patient. Med J Armed Forces India. 2013;69(2):187-189.
- 23. Ravi, K., Srivastava, P., Movdawalla, M., Sen, S., and Kedia, P. 2017. *Implants in glaucoma: a minor review*. Sci J Med & Vis Res Foun. Vol. XXXV:3-9.
- 24. Teruhiko H, Takayasu O, Noriko A, Toshiro Y, and Nobuo I. 2012. *Retinal Photocuagulation Density in the Treatment of Neovascular Glaucoma due to Diabetic Retinopathy*

- 25. Archana S, Premanand C, Raman GV. Aurolab aqueous drainage implant: My surgical technique. Kerala J Ophthalmol 2017;29:41-5.
- 26. Stein JD. *Standard technique for implanting glaucoma drainage devices*. Essentials of Glaucoma Surgery. 1st ed. 2002. New Jersey: Slack Inc.; pp.81-94.